#### REMARKS

The Office Action mailed December 6, 2001, has been received and reviewed. Claims 1 through 21 are currently pending and stand rejected. Claims 1-2, 4-13, and 15-16 have been amended. Claims 3 and 17-21 have been cancelled. Claims 22-27 have been added. With amendment of claims as provided hereinabove, and further in view of the arguments made hereinafter, the applicant contends that Claims 1-2, 4-16 and 22-27 are in condition for allowance and the same is respectfully requested.

#### Objections Under 35 U.S.C. 112, 1st Paragraph

Claims 1 through 21 are objected to for various cited informalities. In view of the amendments to the pending claims, discussed in detail below, applicants submit that the cited informalities have been eliminated and respectfully request withdrawal of the objections to the claims.

Specifically, claims 2, 4, 6, and 7 have been amended to recite "apoptin" and "VP2" instead of "apoptin-like" and "VP2-like." Furthermore, claim 2 has been amended to incorporate all of the limitations of claim 3. The feature of claim 3 has also been incorporated into claims 5 and 7. As a consequence claim 3 has been deleted.

As agreed upon during the examiner interview, the claims were amended to recite a chicken anemia virus protein VP2 in place of any VP2 protein. Pursuant to the Examiner's request, the term "apoptin activity" has been amended to recite "apoptin protein." Also, claims 8-11 have been amended according to the suggestions proposed by the examiner during the interview. As further discussed during the interview, claims 20 and 21 have been deleted without prejudice or disclaimer.

The "use" claims 17, 18 and 19 have been replaced by new "method" claims 22-27. Basis for these new claims can, for example, be found on page 17, line 31-33 or page 28, line 24 and 25.

# Rejections Under 35 U.S.C. 112, 2nd Paragraph

Claims 1-21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claiming the subject matter of the invention.

Applicant has amended claims 1-21 to replace the term "VP2-like activity" with the term "chicken anemia virus protein VP2" and replace the term "apoptin-like activity" with the term "apoptin protein."

Claims 2, 3, 5, and 7 are rejected as being indefinite with respect to the claimed vector system. However, applicants submit that the vector system of claim 1 is clearly defined. The construction of plasmid pCR-VP3mu is described on page 19, line 1 to 24. The sequence of the chicken anemia virus genome and the localization of the chicken anemia proteins VP1, VP2 and VP3 were determined in 1990 and the first application comprising this nucleotide sequence was described in Dutch patent application 9,002,008. Corresponding US Patents also containing such descriptions are, for example, 5,491,073 and 6,162,461. Figure 1 of the US Patent 5,491,073 discloses the complete CAV nucleotide sequence and Figure 3 of US Patent 6,162,461 discloses the DNA and amino acid sequence of VP3. The used nucleotide numbering of all these patents corresponds with each other, hence it is clear that the term "directly upstream of the ATG-initiation codon" means the sequence located directly at the 5' site of the ATG-initiation codon. A figure showing the exact location of "directly upstream" is therefore not necessary.

Pursuant to the Examiner's suggestion, claims 2-16 and 17-21 have been amended to recite "The gene delivery vehicle..." instead of "A gene delivery vehicle..." or are amended to recite "The host cell..." instead of "A host cell..."

#### **INVENTORSHIP**

The present application has been amended to claim priority as a continuation-in-part from U.S. application serial no. 09/740,676. It is noted that the inventors of U.S. application serial no. 09/740,676 (Noteborn and Koch) differ from the inventors of the instant application (09/403,213) (Noteborn and Pietersen). However, Koch is only an inventor of the subject matter pertaining to vaccines in U.S. application serial no. 09/740,676 and is not an inventor of the subject matter relating to apoptosis-inducing capabilities of Apoptin. As such, applicants submit that claiming continuation-in-part status in the present application is proper and respectfully request entry of the same.

Serial No.: 09/403,213

#### Rejections Under 35 U.S.C. § 102

Claims 1, 4, 6, 8, and 9 stand rejected under 35 U.S.C. § 102 as being anticipated by Noteborn et al. (WO 95/03414). As previously discussed, the present application now claims priority to U.S. Patent No. 6,071,520, which is a §371 filing of PCT/NL94/00168, which is a continuation-in-part of 08/030,335, now U.S. Patent No. 5,491,073, which is a §371 filing of PCT/NL91/00165, which has a filing date of September 11, 1991. In view of the foregoing, Noteborn et al. (WO 95/03414), having an effective filing date of September 19, 1994 is not an anticipating reference. Applicants respectfully request withdrawal of the rejection.

#### Rejections Under 35 U.S.C. § 103

Claims 1, 4, 6, 8, and 9 stand rejected under 35 U.S.C. § 103 as being obvious in view of Noteborn et al. (U.S. Patent No. 6,251,433, effective filing date 6/7/95) taken with Zuckermann et al. Claims 1, 6, 8-10, and 12-16 stand rejected under 35 U.S.C. § 103 as being obvious in view of Noteborn et al. (U.S. Patent No. 6,251, 433) taken with Zuckermann et al. and Fallaux et al. Finally, claims 1, 6, 12, 13, 17, and 18 stand rejected under 35 U.S.C. § 103 as being obvious in view of Noteborn et al. (U.S. Patent No. 6,251, 433) taken with Zuckermann et al. and Henderson et al. As previously noted, the present application now claims priority to U.S. Patent No. 6,071,520, which is a §371 filing of PCT/NL94/00168, which is a continuation-in-part of 08/030,335, now U.S. Patent No. 5,491,073, which is a §371 filing of PCT/NL91/00165, which has a filing date of September 11, 1991. In view of the foregoing, Noteborn et al. (WO 95/03414), which is principally relied upon as the basis for all obviousness rejections and having an effective filing date of September 19, 1994, is not an effective prior art reference. As such, applicants respectfully request withdrawal of the rejection.

Serial No.: 09/403,213

## CONCLUSION

In view of the foregoing amendments, and further in view of the arguments made, it is believed that this application is now in condition for allowance. Reconsideration and early notice of allowance is respectfully requested.

Respectfully submitted,

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## VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A gene delivery vehicle comprising a nucleic acid molecule encoding [apoptin-like activity]apoptin protein.

- 2. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 1 additionally comprising a modified translation initiation site directly upstream <u>of</u> the ATG-initiation codon of said nucleic acid molecule, wherein said translation initiation site comprises the nucleic acid sequence GCCAAC.
- 4. (Amended) A gene delivery vehicle comprising a nucleic acid molecule encoding [VP2-like activity]chicken anemia virus protein VP2.
- 5. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 4 additionally comprising a modified translation initiation site directly upstream the ATG-initiation codon of said nucleic acid molecule, wherein said translation initiation site comprises the nucleic acid sequence GCCAAC.
- 6. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 1 additionally comprising a nucleic acid molecule encoding [VP2-like activity]chicken anemia virus protein VP2.
- 7. (Amended) [A]The gene delivery vehicle according to claim 6 additionally comprising a modified translation initiation site directly upstream the ATG-initiation codon of the nucleic acid molecule encoding [VP2-like activity.]chicken anemia virus protein VP2, wherein said translation initiation site comprises the nucleic acid sequence GCCAAC.
- 8. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 1 which is a [virus]<u>viral</u> <u>vector</u>.
- 9. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 8 [which]<u>wherein said viral</u> <u>vector</u> is[a replication-defective virus]<u>replication defective</u>.

Serial No.: 09/403,213

- 10. (Amended) [A]<u>The gene delivery vehicle according to claim 9 [which] wherein said viral vector</u> is an [adenovirus]<u>adenoviral vector</u>.
- 11. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 9 [which]<u>wherein said viral vector</u> is a [retrovirus]<u>retroviral vector</u>.
- 12. (Amended) [A]<u>The</u> gene delivery vehicle according to claim 6 which additionally comprises at least one target molecule.
- 13. (Amended) [A]The gene delivery vehicle according to claim 12 wherein the target molecule is reactive with a tumor cell surface receptor.
  - 14. A host cell comprising a gene delivery vehicle according to claim 13.
  - 15. (Amended) [A]The host cell according to claim 14 which is a helper or packaging cell.
- 16. (Amended) [A]<u>The</u> host cell according to claim 14 which is selected from the group of [HEK;293]<u>HEK-293</u>, [HER;911]<u>HER-911</u>, [PER.C6]<u>PER-C6</u>, Psi-2, and [PA317]<u>PA-317</u> cells.